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09/582,809	06/30/2000	GEORGE E. SEIDEL	XY-LODO-USNP	3161

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,809	SEIDEL ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-12,16,17,19-29,165-167,169,170,172-183 and 185* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-12,16,17,19-29,165-167,169,170,172-183 and 185* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/9/06;10/20/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 20, 2005 has been entered.

Claims 1, 5-12, 16, 17, 19-29, 165-167, 169, 170, 172-183 and 185 are pending. Applicant's arguments and amendments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. In particular, the rejections under 35 USC 103 over Seidel et al (1997) have been obviated by the filing of the 132 Declaration. Additionally, the previous rejections under 35 U.S.C. 112, second paragraph have been obviated by the amendments to the claims. This action contains new grounds of rejection and is made non-final.

Terminal Disclaimer

2. The terminal disclaimer filed on October 20, 2005 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent Nos. 6,071,689, 6,524,860, and 6,372,422 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Information Disclosure Statement

3. The information disclosure statement filed in this application on 10/20/2005 fails to include a concise statement of the relevance of the following non-English language reference listed, as required under 37 CFR § 1.98(a)(3): Ozhin et al (1961); Prokefiew (1983); Solsberry (1966); Wintzer (1982) and Van Munster (1999; Sex Determination by Interferometry). The above items of information have not been considered by the examiner. Additionally, the Pursel et al (1978) reference has not been considered because a copy of these references was not provided (the record provided consisted of only the citation to Pursel et al). The Waggoner et al (1990), Reiling (1997), Rutter (1993), Shackelford (1995) references have not been considered because these references are not readable. The Recktenwald reference has been considered only for the single paragraph overview of "Cell Separation Methods and Applications" on the page entitled "about the book." The other items of information that are otherwise in compliance with the provisions of 37 CFR §1.97-1.98 have been considered by the examiner.

4. Applicant is advised that should claim 1 be found allowable, claim 180 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact

terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-12, 16, 17, 19-29, 165-167, 169, 170, 172-183 and 185 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed does not appear to provide support for the claimed methods of using an insemination sample which is capable of fertilizing eggs "at success levels selected from the group consisting of at least 35%, at least 41%, at least 50%, and at least 90% of a typical unsorted insemination dosage."

Originally filed, now cancelled, claim 2 was drawn to a method for producing a female mammal at success levels selected from the group consisting of at least 35%, at least 41%, at least 50%, and at least 90%." However, the originally filed claim did not recite a comparison between the success levels of the sorted sperm sample and the success levels of a typical unsorted insemination dosage. Accordingly, the originally filed claim does not provide support for the concept of success levels of at least 35% to 90% of a typical unsorted insemination dosage. The success level of a typical unsorted insemination dosage is highly variable, depending on the organism, insemination dosage, # of inseminations, use of superovulation, use of frozen versus nonfrozen sperm etc. For instance, the success rate for an unsorted sample may be 50% (see

Schenk et al, Exhibit A in the response of 10/20/05), in which case a success rate of 35% of the typical unsorted insemination level of 50% is 17.5%. However, there is no basis in the originally filed specification for success levels of 17.5%, or any of the other possible success levels that are expressed as a function of the success levels of a typical unsorted insemination sample.

Additionally, the specification (page 19) states that artificial insemination with 100,000 and 250,000 sperm achieved 41% and 50% pregnancy rates. However, these teachings relate to the pregnancy rates obtained using sorted sperm. These rates do not pertain to pregnancy rates obtained in bovine that are superovulated or bovine that are inseminated with unsorted sperm. Further, the pregnancy rates are absolute numbers, as opposed to the % pregnancy rates compared to a typical unsorted insemination sample.

In Example 1 (page 25), the specification provides the results of a method in which a 3 $X10^5$ dosage of sorted sperm was used to inseminate cows that were not superovulated and in which pregnancy rates of 42% were obtained. Controls had fertilization success levels of 54%. Thereby, the sorted semen provided success levels of 77.7%. However, this disclosure does not provide basis for the claimed method in which the particular levels of success rates are at least 35%, 41%, 50% or 90%. Example 2 (page 26) discloses a method in which bovine were inseminated with 5 x 10^5 unsexed/non-sorted sperm and pregnancy rates obtained "were similar" to those obtained with 10 $x10^6$ sperm. In example 3 (pages 26-27), 1 to 2 $X10^5$ of sex sorted sperm were used for the insemination of heifers that were not superovulated. None of

the females became pregnant when inseminated with sperm shipped at ambient temperature, while 14/29 heifers became pregnant when inseminated with sperm cooled to 5°C during shipping. A comparison of fertilization rates to a typical dosage of unsorted sperm is not provided in this example. In example 4 (pages 27-28), single ovulatory heifers were inseminated with 1 or 2.5 $X10^5$ of sperm cooled to 5°C. Pregnancy rates were 41%, 52% and 56% for 1 $X10^5$, 2.5 $X10^5$ and 2.5 $X10^6$ sperm/inseminate. Thereby, insemination rates were 93% of that of a typical dosage of sperm when $1/10^{th}$ the typical dosage of sperm was used for insemination. Each of the examples set forth in the specification discloses a particular % of success rates, but does not express these success rates as a function of that of a typical unsorted insemination sample. Accordingly, the specification as originally filed does not appear to provide basis for the concept of a method in which fertilization rates are achieved which are at least 35% (36%, 37% etc), at least 41% (42%, 43% etc), at least 50% (51%, 52% etc) or 90% (91% , 92%...to 100%) of the typical unsorted insemination sample.

Additionally, it is noted that while originally filed claim 2 recited a method of producing an mammal wherein the method included the step of fertilizing at least one egg at success levels selected from the group consisting of at least 35%, at least 41%, at least 50% and at least 90%, the specification as originally filed did not provide proper antecedent basis for this subject matter. If Applicant intends to claim the subject matter of original claim 2, then the specification must be amended to provide basis for this subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

6. Claims 1, 5-12, 16, 17, 19-29, and 165-167, 169, 170, 172-183 and 185 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing bovine offspring wherein the methods comprise collecting semen from a bovine, staining the sperm cells in the semen, sorting the sperm by sex chromosomes using a MoFlo flow cytometer / cell sorter at 50 psi using 2.9% Na Citrate as a sheath fluid, collecting the sperm at approximately 500 live sperm/second into tubes containing Cornell Universal Extender (CEU) with 20% egg yolk, and using, within 5-9 hours post-sorting, 3 x 10^5 live, cooled sperm to inseminate bovine that were previously synchronized with prostaglandin F-2 alpha at 12 day intervals, wherein said method results in pregnancy rates of about 80% of controls inseminated using 15.6 X 10^6 motile non-sorted/unsexed sperm (see page 25 of the specification, does not reasonably provide enablement for methods of producing any nonhuman mammal wherein said methods comprise sensing a sex characteristic of sperm cells, sorting sperm cells by any means based on the sex characteristic, generating an insemination sample having a low number of sperm capable of fertilizing at least one egg within a female at success levels comparable to a typical insemination dosage, inserting any portion of the insemination sample into the female, fertilizing at least one egg within the female and producing a nonhuman offspring mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the

nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The claims are broadly drawn to for methods of producing any nonhuman mammal wherein said methods comprise sensing a sex characteristic of sperm cells, sorting sperm cells by any means based on the sex characteristic, generating an insemination sample having a low number of sperm capable of fertilizing at least one egg within a female at success levels comparable to a typical insemination dosage, inserting any portion of the insemination sample into the female, fertilizing at least one egg within the female and producing a nonhuman offspring mammal. The claims in general do not define the step of determining the sex characteristic or separating the sperm based upon the sex characteristics. The claims also recite using "less than about one-half" a typical unsorted insemination sample. But do not recite the actual amount of sperm used for insemination since the claims allow for using any portion of this sample to inseminate a female nonhuman mammal (i.e., step f of "inserting a portion of said insemination sample). It is unclear as to what portion of the sample would be used in the insemination process and in view of the comprising language, it is unclear as to whether additional undefined samples may also be used for the insemination process – i.e., if multiple inseminations with different amounts of sperm may be used. The claims further include methods in which insemination occurs 12 hours after the time that is generally regarded as optimal for a single insemination (claims 10 and 174); methods in

which insemination occurs up to 17 hours or later than about 10 hours after the insemination sample is established (claims 11 and 176, respectively); methods in which the sperm cells are separated at a rate of at least 1200 sorts per second; and methods in which the insemination sample contains at least 60%, 70%, 80% or 90% of sperm having the desired sex characteristic (claims 172, 173, 182 and 183).

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that "(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". In the instant case, specification has not adequately taught one of skill in the art how to practice methods of producing any nonhuman mammal using a low number of sorted sperm and achieving success rates comparable to that obtained with a "typical insemination dosage" for the following reasons.

The claims broadly encompass methods for producing any nonhuman mammal using "less than about one-half the number of sperm" while still achieving success rates comparable to that obtained with a typical unsorted insemination sample. However, the specification provides only one specific example in which such a method has been

accomplished. In particular, example 1, set forth on 25 of the specification, describes a method of using a "low dose" of sex sorted sperm for artificial insemination of a bovine. The method requires collecting a sperm sample from a bovine, staining the sperm cells in the semen, sorting the sperm by sex chromosomes using a MoFlo flow cytometer / cell sorter at 50 psi using 2.9% Na Citrate as a sheath fluid, collecting the sperm at approximately 500 live sperm/second into tubes containing Cornell Universal Extender (CEU) with 20% egg yolk, cooling the sperm sample, and using 3×10^5 live, cooled sperm to inseminate bovine that were previously synchronized with prostaglandin F-2 alpha at 12 day intervals. The sorted sperm were used for insemination within 5-9 hours after sorting and the method resulted in pregnancy rates of about 80% of controls inseminated using 15.6×10^6 motile non-sorted/unsexed sperm. Example 3 of the specification also describes a method of using sex-sorted, unfrozen sperm for insemination purposes. This example states that in one instance insemination with 1-2 $X10^5$ sperm in .1 ml resulted in pregnancy rates of 41% at 8 weeks and in pregnancy rates of 50% at 8 weeks when insemination was performed within 10 hours of the end of sorting.

The specification clearly sets forth the unpredictability in the art of using sex sorted sperm for artificial insemination and particularly of using low-dosages of sex sorted sperm for AI. There are an extensive number of variables which effect the viability of the sperm, the success rate of AI and the pregnancy success rate. For example, at page 3, the specification states that "the sperm are time-critical cells. They lose their effectiveness the longer they remain unused." In Example 3, the specification

teaches that when 38 heifers were inseminated about 22 hours post-sorting, none of the heifers were pregnant 8 weeks after insemination. When inseminations were done 18-29 hours post-sorting, of 33 heifers only 1 remained pregnant at 8 weeks. Additionally, when inseminations were performed 17 to 24 hours post-sorting, only 1 of 7 inseminated females was pregnant at 8 weeks. Accordingly, it is highly unpredictable as to whether sorted bovine sperm samples can be used at time periods of more than 10 or at periods of 17 or more hours post-sorting and still allow for success rates comparable to those obtained with typical inseminations. The specification also emphasizes the unpredictability of using low dosage sex sorted sperm for insemination. The specification defines "low dose" as including levels of 10% to 50% of typical, non-sorted insemination samples. However, the specification exemplifies using low dosages of sex sorted sperm only with bovine animals wherein the dosage is a minimum of 1-3 x 10^5 live, cooled sperm used within 10 hours of sorting. Given the unpredictability in using low dosages of sex sorted sperm for insemination purposes, it is highly unpredictable as to the quantity of bovine sperm or other mammalian sperm that would acceptable to allow for fertilization success rates comparable to those obtained with high dosages of unsorted semen.

The specification (at page 27) also teaches that the handling of the sample post-sorting significantly effects the success of the insemination process. When insemination samples were shipped at ambient temperature, 0 out of 10 females became pregnant. Only when the sperm was cooled to 5C during shipping, was insemination effective.

At page 3-4, the specification discusses additional factors which prevent the hinder the use of sex-sorted sperm. It is stated that "the process through normal flow cytometer techniques may, in fact, be unacceptable for cytometric sorting of sperm cells in certain applications. The sensitivities range from dilution problems and the flow cytometers inherent need to isolate and distinguish each cell individually as well as the pressure sand other stresses which typical flow cytometry has, prior to the present invention imposed upon the cells or other substances that it was sorting. This may also represent a unique factor for sperm cells because it appears that even though the sperm cell may appear to pass through the flow cytometer and be sorted with no visually discernable side-effects, in fact, the cells themselves may have been stressed to the point that they perform less optimally in the insemination process." While this passage appears to state that these problems occurred only prior to the present invention, the specification and claims do not recite any particular advancements which allow for the ordinary artisan to overcome each of these problems when sorting sex from any organism, using any means for sensing a sex characteristic, any means for separating the sperm, any means for collecting the sperm, any means for storing and transporting the sperm, any low dosage of sperm and any means of artificial insemination. The specification teaches that the sorting rate and pressure used to run the flow cytometer may significantly effect sperm viability. However, the majority of the claims allow for the use of any type of apparatus to sense the sex characteristic and to separate the sperm cells based on the sex characteristic. The specification does not provide sufficient guidance to enable the skilled artisan to use any apparatus under any

conditions, and particularly under any conditions of pressure or sort rate, to generate insemination samples that achieve fertilization rates comparable to those obtained with unsexed, unsorted sperm cells.

The specification further teaches that the selection of a sheath fluid greatly influences the viability of the sperm cells. For instance, at page 12, the specification teaches that "the stress imposed by handling of the cells within the flow cytometer appears significant for this application...For instance, while it has been known to utilize fluids having a proper pH factor or osmoality, the present invention recognizes that there may be certain chemical compositions to which the cells may be hyper-responsive. These hyper-responsive chemical compositions may naturally vary based upon the cells or even the prior handling of the cells." The specification goes on to teach a specific citrate-based sheath fluid for sorting bovine cells and a HEPES-based sheath fluid for sorting equine cells. However, the specification does not teach chemical compositions that are suitable for sorting other types of mammalian sperm. As set forth in the specification, a sperm cells response to a chemical will vary depending on the type of chemical, source of sperm cell and previous handling of the sperm cells. The identity of the chemicals that cause stress to sperm cells from other bovine, equine and other mammals can only be determined through experimentation. There is no predictable means for determining a priori which sheath fluids will impose minimal stress on the sperm cells and allow for the sorting of sperm cells to generate an insemination sample that can be used to fertilize eggs at the same success level as a typical insemination sample. In particular, with respect to claims 27 and 177, the

specification has not enabled using any HEPES sheath fluid for the sorting of any type of sperm cell. The specification has stated that it is unexpected that HEPES-based HBGM3 solution was effective as a sheath fluid during the sorting of equine sperm. The specification has not taught that this solution can be used with other sperm cells or that other HEPES solutions can be used with equine or other types of sperm cells. In view of the unpredictable effects that chemical compositions may have on the viability of sperm cells, undue experimentation would be required to practice the methods of claims 27 and 177 as they are broadly claimed.

Other factors which influence sperm viability include different aspects of the collection process. At page 15, the specification teaches that "it may be important that the container which makes up the collector be properly sized so that it acts as some means of avoiding an impact between the cells and the container itself." The specification also discusses the criticality of selecting a proper collection fluid in order to reduce stress to the sperm cells.

The specification further teaches that the dilution process may effect the success rate of the insemination process. At page 21 of the specification, it is stated that "It has been discovered that dilution may create an effect upon the sperm cell's viability and so it may be appropriate to avoid too large a level of dilution by providing a smaller sample." However, the specification does not teach what would constitute an appropriate level of dilution or appropriate type of dilution solution for diluting the sperm of the wide array of non-bovine mammals encompassed by the claims and does not provide sufficient guidance for selecting alternative dilution levels and solutions for non-

bovine sperm samples. The unpredictability surrounding the insemination process is highlighted by the passage at page 22: "The utilization of embryo transfer equipment may be used because there may be high sensitivity of the uterine wall for such low dose, sexed inseminations." Yet, the specification does not clarify which mammals require or do not require the utilization of embryo transfer equipment.

With respect to claim 23, the step of staining the sperm cells is also known to be critical in influencing the viability of the sperm and effectiveness of the sorting procedure to obtain viable sperm. Responsiveness to stain also varies depending on the type of stain. The specification (page 20) teaches that higher amounts of stain might "to some extent" provide better results. The specification teaches using a solution of 38uM Hoeschst 33342 stain. The specification does not specifically exemplify improved results using this concentration of stain. Claim 23 allows for the use of any stain, as long as it is present at a concentration of 38uM. However, the specification does not teach any stains other than Hoeschst 3342 that can be used at this concentration. In view of the unpredictability as to how a stain and the concentration of stain will effect the viability of sperm cells and the sorting process, undue experimentation would be required to practice the claimed invention using any stain at a concentration of 38uM.

Additionally, the ability to apply the claimed sorting and insemination method to non-bovine mammals is highly unpredictable. The specification does not provide any specific examples of using low doses of sex sorted sperm for insemination in non-bovine animals. Given the variability in sperm viability in different species and the variability in sorting success and insemination success in different species, it is highly

unpredictable as to whether the results obtained with bovine can be extended to other species. The unpredictability in applying the claimed invention to non-bovine mammals is emphasized by the teachings in the specification. At page 4, the specification states that "artificial insemination with a high success rate is one of a statistical nature in which a multitude of factors seem to interplay. Thus, solutions proposed to some degree involve a combination of factors which, when thoroughly statistically studied, will be shown to be necessary either in isolation or in combination with other factors. Such a determination is further compounded by the fact that **the results vary by species** and may be difficult to ascertain due to the fact that testing and statistical sampling on a large enough database is not likely to be worth the effort at the initial stages." Yet, the specification does not provide any specific guidance as to what particular combination of factors/conditions would be required to obtain comparable success rates in non-bovine, non-human mammals. Additionally, the teachings of Johnson (cited in the IDS; Journal of Reproduction and Fertility, 1997) highlight the unpredictability of using low dosage sex sorted sperm in other mammals. Specifically, Johnson (page 262) teaches that "It is unlikely that the technology for small numbers of spermatozoa from cattle will be directly applied to swine because of the anatomy of the pig uterus which provides an impediment to small numbers of spermatozoa." The specification does not particularly address this limitation and does not provide any particular guidance as to how to overcome this obstacle when inseminating pigs or other mammals having a uterus of similar anatomy. Furthermore, Cran (Theriogenology, January 1997) also emphasizes the unpredictability of using low doses and/or sex sorted semen for insemination. Cran

teaches that pregnancy rates of lambs were low when sex sorted semen was used for insemination. In one study, 0 of 18 ewes inseminated with low doses of X sperm lambed, while 5/12 inseminated with unsorted sperm produced lambs. In a second study, none of 5 ewes inseminated with low dose Y sperm lambed; 4/25 inseminated with low dose X sperm lambed; and 2/30 inseminated with unsorted low dose sperm lambed. Cran states that the low pregnancy rates may be due to a combination of delay between semen collection and insemination, asynchrony between insemination and ovulation, semen doe and the onset of seasonal anestrus. However, the specification and prior art do not provide any specific guidance as to how to modify the method of Cran so as to predictably generate a method in which low doses of ram semen can be used to produce fertilization rates equivalent to that obtained when using high doses of unsexed sperm. It is unpredictable as to how the methodology would need to be modified in order to effectively perform low dosage AI with sex sorted sperm in other mammals, including elephants, whales, gorillas, pandas etc. The teachings in the specification regarding bovine do not provide sufficient guidance to enable the use of this technology in other mammals because it is unclear as to how the viability of the sperm will be effected by the rate and pressure of the sorting process, the sheath fluid used for the sorting process, the collection fluid and collection container, the dilution process, the freezing process, and the type of insemination procedure.

Accordingly, the specification emphasizes the unpredictability in the art of using low dose sex-sorted sperm for AI and teaches that a multitude of factors interact in undefined ways to influence the viability of the sorted sperm and the success rate of

insemination. However, the specification teaches only one particular set of conditions – i.e., the conditions set forth in Example 1 - that were shown to be effective for achieving success rates with low dose sex-sorted sperm comparable to success rates achieved using a typical high dosage, nonsorted insemination sample. Sufficient guidance is not provided in the specification as to how to modify the conditions set forth in Example 1 and maintain a success rate that is about 80% of the success rate achieved with typical insemination samples. Additionally, sufficient guidance is not provided in the specification as to how to apply the methodology used with bovine to all other non-human mammals. The genus of non-human mammals is significantly large and includes a vast multitude of animals whose sperm has not been previously studied for its ability to be sorted, for its sensitivity to chemicals and the sorting process, for its sensitivity to handling and freezing processes or for its ability to be used for insemination purposes. Accordingly, extensive experimentation would be required to practice the claimed invention using other sorting and insemination conditions for bovine sperm or using sperm from non-bovine, non-human mammals.

With respect to claims 172, 173, 182 and 183, the specification does not reasonably provide enablement for methods of producing any non-human mammal using an insemination sample having a plurality of spermatozoa wherein up to 100% of the spermatozoa have the same sex determination characteristic. The ability to sort sperm from any nonhuman mammal on the basis of a sex determination characteristic such that the resulting sample can be used for fertilization to reproducibly generate offspring in which 90% of more of the offspring are female is highly unpredictable. This

unpredictably is exemplified by the results set forth in the specification. In particular, Seidel (Theriogenology, 1997; see abstract) teaches that fourteen of 17 calves (82%) born from sex-sorted sperm were of the selected sex. The specification does not provide any examples in which spermatozoa were sorted to rates up to 100%. The prior art of Rens (US Patent 5,985216, issued 1999) does teach that bovine sperm can be sorted to purities of about 90%. Rens also teaches that under some conditions, porcine sperm could be sorted to a purity of 92% for sperm bearing the Y chromosome. However, there is no specific guidance provided in the specification for how one may accomplish the sexing of sperm to achieve purity rates of 95%, 99% or 100% in bovine and other non-bovine mammals. It is unpredictable as to whether one of skill in the art could sort sperm from these mammals at purity rates of above 90%. The unpredictability of sorting sperm to high levels of purity, including purity levels above 90% is supported by the teachings in the art. For example, Fugger (1999; cited in the IDS) teaches that the ability to effectively sort sperm cells varies with species as a function of the shape of the sperm and the magnitude of difference in DNA content between X and Y chromosomes. Additionally, Johnson (1992, page 13; cited in the IDS) teach the difference in DNA content between X and y chromosome bearing sperm for several organisms, including turkey (0% difference), human (2.9% difference) and rabbit (3% difference). Johnson also reports that rabbit sperm were sorted to purities of 86% for X-chromosome bearing sperm and 81% for Y-chromosome bearing sperm. The specification has not taught that a representative number of non-human mammals have sperm of an acceptable shape and having an acceptable difference in the DNA content

of their X and Y chromosomes to allow for the sorting of sperm at levels of more than 60, 70, 80 or 90%. There are no teachings in the prior art as to how to overcome the problems associated with a lack of difference in the DNA content between X and Y-chromosome bearing sperm or the challenges imposed by the shape, morphology and heterogeneity of sperm. The specification does not provide sufficient guidance as to how to sort sperm from non-bovine, non-porcine mammals to purity levels of 90% or above or how to sort sperm from bovine and porcine animals to up to 100% purity. It is unpredictable as to what methodologies should be employed to achieve these high purity levels and in the absence of specific guidance provided by the specification or prior art, undue experimentation would be required to achieve these purity levels.

For the reasons set forth above and in view of the high level of unpredictability in the art and the lack of specific guidance provided in the specification, undue experimentation would be required to practice the invention as it is broadly claimed.

Response to arguments:

In the response, Applicants state that the amendment to the claim to recite a "typical unsorted insemination dosage" is believed to address much of the enablement concerns. However, the rejection was not based solely on the absence of such a recitation. The rejection addresses numerous points regarding the lack of enablement of the claims and thereby is maintained for the reasons stated above.

The response further states that the 132 Declaration of John Schenk has been provided to address any remaining enablement concerns.

The 132 Declaration of John Schenk has been fully considered but is not sufficient to overcome the present grounds of rejection. It is noted that the declarant is an employee of XY Inc., an assignee of the present application. Further, the declarant is co-inventor of 09/001,394 and 09/015,454, to which the present application claims priority.

The declaration states that the "methods and apparatus necessary to enable a person of ordinary skill in the art pertaining to sexing spermatozoa and producing animals from such spermatozoa to accomplish the separation rates and success levels recited in the claims." However, the present claims are not directed to methods which require the use of any particular apparatus. Accordingly, the declaration is directed to limitations that are not recited in the claims. Further, the declaration is vague in its statement regarding the methods necessary to achieve the claimed success rates using dosages of sperm that are one half that of a typical dosage of sperm. The declaration points to a number of techniques that are discussed in the specification which may be useful in reducing the adverse stress effects. However, the declaration does not specify which of the vast array of methods disclosed by the specification are capable of achieving the claimed success rates. Each of the present claims recites a different combination of techniques and different aspects of these techniques. There are no claims limited to the specific embodiments exemplified in the specification in which the high speed flow sorting method was used in combination with low dosages of sperm to achieve the stated fertilization levels. It is unclear from the arguments and declaration and from the originally filed specification as to which particular combinations of

techniques are critical for practicing the claims invention and achieving the asserted success rates. For instance, the specification indicates that the sperm cells are highly sensitive, that sperm from each type of organism may respond differently to different chemical environments (e.g., HEPES solution versus Citrate solution), that sorting, handling, and freezing process damage sperm, and that it is extremely difficult to obtain sufficient quantities of sorted sperm that are not damaged and which can be used for successful artificial insemination procedures. Yet, the claims are not limited to methods which utilize any particular combination of techniques which overcome the problems associated with the sorting, handling and freezing process. The specification does not provide sufficient guidance as to which particular combinations of parameters/factors may be employed to obtain the success rates recited in the claims.

Further, the claims encompass methods in which sperm sorted by high speed flow cytometry are used to artificially inseminate any nonhuman mammal. However, the teachings set forth in the specification are limited to bovine. The declaration and response do not address the enablement rejection as it applies to methods of artificially inseminating any nonhuman mammal. Again, it is noted that Cran teaches that 0/18 ewes inseminated with low doses of X sperm lambed. In a second study by Cran , 0/5 ewes inseminated with low dose Y sorted sperm lambed, and only 4/25 inseminated with low dose X sorted sperm lambed.

The specification teaches only one particular set of conditions – i.e., the conditions set forth in Example 1 - that were shown to be effective for achieving success rates of 80% with bovine low dose sex-sorted sperm. Sufficient guidance is not provided

in the specification as to how to modify the conditions set forth in Example 1 and obtain a success rate that is at least about 90% of the success rate achieved with a typical unsorted insemination samples for any non-human mammal. The specification has not established that a wide variety of conditions can be used or obtained by routine experimentation to allow for the sorting of sperm from non-bovine mammals in order to obtain success rates from 35%, 41%, 50%, or at least 90% of that obtained with a typical unsorted insemination sample. Accordingly, it is maintained that in view of the high level of unpredictability in the art and the lack of specific guidance provided in the specification, undue experimentation would be required to practice the invention as it is broadly claimed.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103□ and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 8, 19, 16, 17, 25, 28, 165, 167, 169-170, 172-183 and 185 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (1996) in view of Rens (U.S. Patent No. 5,985,216).

Seidel teaches methods for making bovine mammals comprising sorting sperm cells according to sex using flow cytometry wherein the sperm cells are sorted to purity rates of about 90%, establishing an insemination sample, inserting a low dosage (1-2 X 10^5 in .1 ml) of sorted sperm cells into the uterine horns of the female bovine after the onset of estrus; and fertilizing the eggs of the bovine so as to produce at least one offspring of the desired sex. Seidel teaches that 11 of 22 females inseminated with sperm cooled to 5C during shipping were pregnant at 8 weeks. In view of the teachings in the specification, this is considered to be a success level comparable to a typical insemination dosage. The sperm were deposited deep in the uterine horn ipsilateral to the ovary with the largest follicle being determined by ultrasound.

Seidel does not specify the rate of sorting and specifically does not teach sorting sperm at rates of 1200 sorts/second or operating a flow cytometer at 5-50 KHz.

Rens teaches a method of high speed flow cytometry for sorting sperm. In the method of Rens (see columns 4-6), a sample of sperm is obtained from a male mammal, the sperm is stained with Hoeschst 33342 dye in order to distinguish between viable and nonviable sperm (column 5, lines 4-10), the sperm are sorted in a high speed flow cytometer using a nozzle that forms a stable droplet containing each individual sperm cell (column 2, lines 23-32), the sperm are sorted according to their sex characteristics and isolated populations of X- and Y-chromosome bearing sperm are

collected. Rens teaches sampling rates of 500 sperm/second and 2000 sperm/second (column 6). Further, the nozzle allowed for sample rates up to at least 15,000 sperm/sec (column 4, lines 29-31). Rens states that the "high level of performance is beneficial for efficient sperm sorting." Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to have used sorting rates of about 500 sperm/sec or 1200 sperm/second in order to have allowed for the faster sorting of sperm so as to have provided adequate quantities of sex-sorted samples that could be used for the insemination process.

Rens does not specify operating the high speed cell sorter at 5-50 KHz. However, methods for sorting sperm using high speed cell sorters were well known in the art at the time the invention was made and the parameters which would effect the sorting process were also well known. To determine the optimum conditions for performing a method step is well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller,* 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955). Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected the optimum conditions for operating the flow cytometer, and thereby to have operated the flow cytometer within a range of 5-50 KHz depending on the rate of sorting, type of sperm, etc, in order to have provided the most effective means for sorting the sperm.

Regarding claims 178 and 179, Rens does not specify the size of the collection container. However, it would have been well within the skill of the art at the time the invention was made to have selected a collection container of an appropriate width in order to have prevented damaging the sperm since Rens does teach the criticality of the dimensions of the sorting device and the orientation of the sperm within the sorting device in order to maintain sperm viability (see, for example, column 3).

Regarding claim 177, Seidel teaches that the semen are collected in HEPES-buffered extender and transported to the location at which they are sorted by flow cytometry. In view of the conventionality of using HEPES buffered mediums for collecting and diluting bovine sperm, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a sheath fluid containing a HEPES-buffered medium since such a sheath fluid would have been expected to have provided an effective chemical environment for the sorted sperm.

8. Claims 5, 7, 9, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (1996) in view of Rens, as set forth above, and further in view of Seidel (1995).

The teachings of Seidel (1996) are presented above. Seidel teaches insemination deep into the uterine horn ipsilateral to the ovary. Seidel does not teach insemination both ipsi and contra-lateral within the uterine horns.

However, Seidel (1995) teaches ipsilateral and contra-lateral insemination of low dose semen into females. The reference teaches that pregnancy rates were nearly identical for ipsilateral and contra-lateral insemination.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (1996) so as to have performed the insemination procedure by inserting the semen both ipsi and contra-lateral into the uterine horns because this would have provided an equally effective means for inseminating female bovine.

9. Claims 19-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (1996) in view of Rens, as set forth above, and further in view of Seidel (Theriogenology (1994) 41: 168).

The teachings of Seidel (1996) and Rens are presented above. The combined references do not teach superovulating the females prior to insemination.

Seidel (1994) teaches methods for stimulating superovulation in cows. In the method of Seidel, cows are treated twice a day at 12 hour intervals with injections of 6, 6, 4, 4, 2, 2, 2, and 2 mg FSH and given three dosages of prostaglandin of 25 mg and 12.5 mg PGF-2-alpha on days 6 and 7, respectively, of FSH treatments. The superovulation treatment is initiated starting between days 9 and 14 of the estrous cycle.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel so as to performed the surgical insemination procedure on females that were superovulated and synchronized using the FSH/PGF-2-alpha treatment methods as disclosed by Seidel (1994) in order to have achieved the benefit of providing a more effective and convenient means of insemination since the females could then be inseminated at the most optimal time

during estrous and the timing of the insemination procedure could be scheduled to correspond with the collection and sorting of sperm.

10. Claim 166 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seidel (1996) in view of Rens, as set forth above, and further in view of Rath (Theriogenology (1997) 47: 75-800; cited in the IDS) and Seidel (1995; cited in the IDS).

The teachings of Seidel and Rens are presented above. The combined references do not specify the solution into which the sperm cells are collected and thereby do not teach collecting the sorted sperm in a citrate solution containing about 6% egg yolk.

However, Rath (page 796) teaches collecting sex-sorted sperm into a collection media composed of TEST extender containing 2% hen egg yolk. Thus, Rath teaches the concept of collecting sperm sorted cells into a sperm extender medium. Additionally, Seidel (1995) teaches extending sperm in Cornell Universal Extender which is known to contain citrate and egg yolk. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Seidel (1996) so as to have collected the sperm in an extender comprising a citrate solution and egg yolk in order to have sorted the sperm into a medium that would help to preserve the sperm and/or which could be used for subsequently freezing of the sperm.

Response to arguments:

In the response, Applicants traversed the 103 rejections over Seidel (1996) by arguing that the sampling rates of Rens are not the same as the rates of separating

sperm set forth in the present claims. The response states that a sampling rate is distinct from a sorting rate in that a sampling rate refers to the number of analysis events, whereas a sorting rate refers to the actual number of sperm sorted per second. Applicants conclude that the combination of references "cannot support an obviousness concern with respect to Applicant's claims reciting 'separating nonhuman sperm cells based upon said sex characteristics and a rate of at least 1200 separations per second."

This argument has been fully considered but is not persuasive. While it is agreed that Rens does not specify the sampling rate, the information provided by Rens does indicate that the method of Rens and the sorting apparatus of Rens, as well as the sorting apparatuses known in the art at the time the invention was made, can be used to achieve sampling rates equivalent to that of the claimed invention. The present claims recite a method in which the separation rates are "at least 1200 separations per second." Rens (col. 6) exemplifies methods using sampling rates of 2000 sperm/second and teaches that the nozzle allowed for sample rates of up to at least 15,000 sperm/second. If the proper orientation is achieved for 60% of the sperm (note that Rens teaches that the correct orientation is achieved in excess of 60% of sperm), then the rates of sorting in the method of Rens would be at least 1200 sorts/sec (for sampling rates of 2000sperm/sec) or 9000 sorts/sec (for sampling rates of 15,000 sperm/sec).

The response further states that the 132 Declaration of John Schenk has been provided to establish the unexpected results obtained when using separation rates of

1200 sorts/sec, while maintaining fertilization success levels of at least 35% of that obtained with a typical unsorted artificial insemination sample.

The 132 Declaration of John Schenk has been fully considered but is not sufficient to overcome the present grounds of rejection. The declaration states that "I am not aware of and do not believe the prior art has disclosed achieving success levels at such separation rates prior to the current invention." However, the present rejection has been made under 35 U.S.C. 103, rather than 35 U.S.C. 102. Thereby, there is no requirement for the prior art to specifically exemplify the claimed invention.

The declaration further states that the "methods and apparatus necessary to enable a person of ordinary skill in the art pertaining to sexing spermatozoa and producing animals from such spermatozoa to accomplish the separation rates and success levels recited in the claims." However, the present claims are not directed to methods which require the use of any particular apparatus. Thereby, any unexpected results obtained using such an apparatus are not applicable to the present claims. Further, the declaration is vague in its statement regarding the methods necessary to achieve the claimed success rates using dosages of sperm that are one half that of a typical dosage of sperm. The declaration points to a number of techniques that are discussed in the specification which may be useful in reducing the adverse stress effects. However, the declaration does not specify which of the vast array of methods disclosed by the specification are capable of achieving the claimed success rates. Each of the present claims recites a different combination of techniques and different aspects of these techniques. There are no claims limited to the specific embodiments

exemplified in the specification in which the high speed flow sorting was used in combination with low dosages of sperm to achieve the stated levels of success rates.

The declaration states that high speed sorting places stresses upon the sperm cells and thereby may compromise the fertilization process. However, those of ordinary skill in the art at the time the invention was made were well aware of the stresses that high speed sorting makes on the sperm. The ordinary artisan was also aware of methods which could be used to reduce these stresses and improve the overall efficiency of the artificial insemination process. The question regarding the present rejection is whether it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used high speed flow sorting in combination with low dosages of sperm. As set forth in the rejection, this combination of techniques would have been obvious to one of ordinary skill in the art because such a combination would have allowed for the faster sorting of sperm so as to have provided adequate quantities of sex-sorted samples that could be used for the insemination process. Applicant's response and declaration do not point to any particular teachings in the art which specifically teach away from this combination and which provide a factual basis for why the combination would not be effective to the degree required by the claims. The present claims are inclusive of methods in which fertilization rates of 35% of that of the typical unsorted artificial insemination sample are achieved. As discussed in the Schenk 2000 reference (Proceedings of the 18th Technical Conference on Artificial Insemination and Reproduction; Exhibit A in the response of 10/20/05), pregnancy rates in bovine are in the range of 50% to 60% with unsorted insemination samples. Thereby,

the claims encompass methods in which a 17.5% success rate is achieved. There is no clear statement in the declaration or arguments or evidence provided to establish that this success rate would have been unexpected.

As set forth in the MPEP 716.02, the burden is placed on Applicant to establish that "the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." *Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992).* There must be a clear nexus between the asserted unexpected results and the method steps that allow for the unexpected results. Further, the claims must be commensurate in scope with the aspects of the invention which allow for the asserted unexpected results. In the present situation, the declaration is general in nature and points only to the wide variety of possible techniques and apparatuses disclosed in the specification and states by using some combination of these techniques and apparatuses, one could achieve unexpected improve results. However, neither the response nor the declaration establish a clear nexus between the claims as they are broadly written and any asserted unexpected results.

Regarding claim 177, the response further states that the claim requires the use of a HEPES-buffered medium as a sheath fluid. It is asserted that Seidel does not teach this aspect of the claimed invention. However, Seidel does teach collecting semen in HEPES-buffered extender and sorting the resulting semen samples. Accordingly, the use of a HEPES buffered medium for bovine sperm would have been obvious to one of ordinary skill in the art given the use of this buffer for collection and dilution of bovine sperm. The response further states the specification sets forth the unexpected results

obtained when using HEPES buffered medium as a sheath fluid. However, the present claims are not limited to methods of sorting equine sperm. Rather, the present claims encompass the sorting of either bovine or equine sperm. Also, the specification has not established any unexpected results obtained using any concentration or formulation of HEPES buffered medium. The response further states that "use of a hepes buffered medium may be considered unexpected, in as much as the hepes substance originally was developed for bovine applications, as noted in the specification." The specification at page 14 states that the HEPES buffer HBGM3 was well known in the art for bovine applications. Thereby, the specification acknowledges that that the use of HEPES buffer in flow sorting was well known in the art at the time the invention was made.

Regarding claims 178 and 179, the response states that the cited prior art does not teach utilizing a container having a diameter of at least 15 mm or using a collection container having stream matched physical characteristics. However, Rens does teach the criticality of the dimensions of the sorting device and the criticality of the orientation of the sperm within the sorting device in order to maintain sperm viability (see, for example, column 3). According, it would have been well within the skill of the art at the time the invention was made to have selected a collection container of an appropriate width in order to have prevented damaging the sperm. The response does not set forth why the use of any collection device greater than 15mm would have been unobvious. Further, the specification does not set forth any specific improved results obtained with collection devices having a diameter greater than 15mm which would thereby suggest that use of such a container would be unobvious. Rather, the specification speculates

on the advantages of such a container, stating, for example, that "it may be important that the container which makes up the collector be properly sized so that it acts as some means of avoiding impact between the cells and the container itself; "Perhaps merely providing a wide opening to the container which serves as part of the collector (14) may be sufficient"; "designing a collection container which matches the geometry of the stream...may be most optimal (pages 15 and 16; emphasis added).

THE FOLLOWING ARE NEW GROUNDS OF REJECTION:

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 5-12, 16, 17, 19-22, 24-29, 165, 167, 169-170, 172-183 and 185 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 138-145 of U.S. Patent Application No. 09/744,675. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '675 are both drawn to methods for producing a nonhuman mammal wherein the methods comprise

collecting sperm cells from a male, establishing a cell source which supplies sperm cells, sorting sperm cells so as to separate the sperm cells according to sex, inserting a portion of the sperm cells into a female and fertilizing at least one egg of said female. The present claims differ from the claims of '675 in that they are limited to methods for establishing an artificial insemination sample from any nonhuman mammal, whereas the methods of '675 are broadly drawn to methods for establishing an artificial insemination sample containing sperm cells from an equine. Since equine constitute a nonhuman mammal, the species set forth in the claims of '675 anticipates the claimed invention. Further, the present claims and the claims of '675 are both inclusive of methods in which high speed flow cytometry is used to separate sperm cells at a rate of at least 1200 sperm/s (i.e., greater than 900 sperm/s as recited in the claims of '675). The instant claims and the claims of '675 also are inclusive of methods in which the sheath fluid contains a HEPES buffered medium, methods in which a low dose of sperm cells is utilized and methods in which fertilization success rates of from 35% to 90% of that of a typical unsorted insemination dosage are achieved.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims 1, 2, 5-12, 16, 17, 19-22, 24-29, 165, 167, 169-170, 172-183 and 185 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 124-141 of U.S. Patent Application No. 10/081,955. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '955 are both

drawn to methods for producing a nonhuman mammal wherein the methods comprise collecting sperm cells from a male, establishing a cell source which supplies sperm cells, sorting sperm cells so as to separate the sperm cells according to sex, inserting a portion of the sperm cells into a female and fertilizing at least one egg of said female. The present claims differ from the claims of '955 in that they are limited to methods for establishing an artificial insemination sample from any nonhuman mammal, whereas the methods of '955 are broadly drawn to methods for establishing an artificial insemination sample containing sperm cells from an equine. Since equine constitute a nonhuman mammal, the species set forth in the claims of '955 anticipates the claimed invention. Further, the present claims and the claims of '955 are both inclusive of methods in which high speed flow cytometry is used to separate sperm cells at a rate of at least 1200 sperm/s (i.e., greater than 900 sperm/s as recited in the claims of '955). The instant claims and the claims of '955 also are inclusive of methods in which the sheath fluid contains a HEPES buffered medium, methods in which a low dose of sperm cells is utilized and methods in which fertilization success rates of from 35% to 90% of that of a typical unsorted insemination dosage are achieved.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

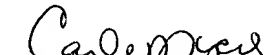
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach

the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)-272-0735.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
April 26, 2006



CARLA J. MYERS
PRIMARY EXAMINER